09	120	180	240	300
GTCCTTCCACCATGCACTCGCTGGGCTTCTCTGTGGCGTGTTCTCTGCTGCCGCTG 1+++++++	CGCTGCTCCCGGGTCCTCGCGAGGCGCCCCCCCCCCCCC	ACCTCTCGGAGGCCCGACGCGGGCGAGGCCACGGCTTATGCAAGCAA	AGGAGCAGTTACGGTCTGTGTCCAGTGTAGATGAACTCATGACTGTACTCTACCCCAGAAT 181+++++++	ATTGGAAAATGTACAAGTGTCAGCTAAGGAAGGAGGCTGGCAACATAACAGAACAGG 241+++++++-
				•

FIG

CCAACCTCAACTCAAGGACAGAGAGAGACTATAAAATTTGCTGCAGCACATTATAATACAG

MATCH WITH FIG.

360	420	480	540	009	. 099
MATCH WITH FIG. 1A GGTTGGAGTTGAGTTCCTGTTCTCTGATATTTTAAACGACGTCGTGTAATATTATGTC N L N S R T E E T I K F A A A H Y N T E	AGATCTTGAAAAGTATTGATAATGAGTGGAGAAAGACTCAATGCATGC	GTATAGATGTGGGGAAGGAGTTTGGAGTCGCGACAAACACCTTCTTTAAACCTTCCATĢTG 	TGTCCGTCTACAGATGTGGGGGTTGCTGCAATAGTGAGGGGCTGCAGTGCATGAACACCAAAAAAAA	SCACGAGCTACCTCAGCAAGACGTTATTTGAAATTACAGTGCCTCTCTCT	AACCAGTAACAATCAGTTTTGCCAATCACACTTCCTGCCGATGCATGTCTAAACTGGATG
301	361	421	481	541	601

MATCH WITH FIG.

	CACAGACATTTTTGTTGAGAGGGGTCGGTTACACCCCGGTTGGCTTTAAACTACTTT MATCH WITH FIG. 1D FIG. 1C	
1020	GTGTCTGTAAAACAAACTCTTCCCCAGCCAATGTGGGGGCCAACCGAGAATTTGATGAAA	961
	GCCCCGAAGCCGGACGGTCGACACCTGGGGTGTTTCTTGATCTGTCTTTGAGTACGGTCA GCCCCCGAAGCCGGACGGTCACCTGGGGTGTTTCTTGATCTGTCTTTGAGTACGGTCA G L R P A S C G P H K E L D R N S C Q C	901
096	CGGGGCTTCGGCC	0
. 006	ATGACATCTGTGGACCAAACAAGGAGCTGGATGAAGAGACCTGTCAGTGTGTCTGCAGAG 1+++++++	841
) 	ACCGAGTCCTTCTAAAA	18/
840		. 6
780	721+++++++-	72
	AAATGTCTGTTCAA Y R Q V AGGCAGCGAACAAG	
720	TTTACAGACAAGTTCATTCCATTATTAGACGTTCCCTGCCAGCACACACTACCACAGTGTC	661

1 瓦

MATCH WITH FIG.

MATCH WITH

E F D E N -	ACACATGCCAGTGTATGTAAAAGAACCTGCCCCAGAAATCAACCCCTAAATCTGGGAA	TGTGTACGGTCACATATTTTTTTTGACGGGGTCTTTAGTTGGGGATTTAGGACCTT T C Q C V C K R T C P R N Q P L N P G K -	AATGTGCCTGTGAATGTACAGAAAGTCCACAGAAATGCTTGTTAAAAGGAAAGAAGTTCC	TTACACGGACACTTACATGTCTTTACGAACAATTTTCCTTCTTCAAGG C A C E C T E S P Q K C L L K G K K F H -	ACCACCAAACATGCAGCTGTTACAGACGGCCATGTACGAACCGCCAGAAGGCTTGTGAGC 	SCYRRCGIACAIGCIIGGCGGICIICCGAAACACACC	CAGGATTTTCATATAGTGAAGAGTGTGTCGTTGTGTCCCTTCATATTGGCAAAGACCAC	GTCCTAAAAGTATATCACTTCTTCACACACACACAGGAAGTATAACCGTTTCTGGTG G F S Y S E E V C R C V P S Y W Q R P Q -	AAATGAGCTAAGATTGTACTGTTTCCAGTTCGATTTTCTATTATGGAAAACTGTGT
ĸ	ACCC	11GG	AAAA	TTTI K	CCAG) 5 0	ATAT	rata Y	ATTA
z	ATCA	ragt Q	rgtt	CAA		ا ا ا	TTC	S	TCT/
& U	GAA	CTT	GCT	CGAZ	CGAA	7 7 7	ויכככ	4GGG	ATTT
r)	CCA	GGT R	AAT	TTA	GTA		GTG	CAC2 V	TCG?
σ.	TGCC	ACGC	CAGA	GTCI	CCAT +	ξ () ()	GTT	SCAA	rtca
S Q C	ACC	TGG.	CCA	GGT(CGG(א ה ה	TGTC	ACAC C F	CAGI
Д	AAGA	rtct R	AAGT	rtca S	PAGA	T H	GTG	CAC	TTC
ניי	TAAI	ATTS K	AGAJ	TCT	TTAC +	7 X	AGAA	rctt E	rgrī
IJ	ratg	TAC	STAC	T	CTG		TGA	ACT'	TAC
×	GTG1	CACA	AATG	rtac C	3CAG	S	ATAG	ratc S	ATTG
Z	AGT	TCA	GTG	CAC	CAT((1) (1)	CAT	GTA1 Y	AAGA
X	SCC	0 0 0 0 0	CCT	7-7 GGA C	AAA 	- [-	TTT(AAA(S	GCT
O >	ACACATGCCAGT	TGTGTACGGTCA T C Q C	AATGTG	TTACACGGACAC C A C E	ACCACCAAACAT	H Q T C			AAATGA(
	1001	1701	0	1001	1141		1201	·	-

WITH FIG.

MATCH

5/47

1500 1440 1380 1560 1620 **ITTCAGACAGAAGGACTTGGTACACCTATTGAAATGTCTTTACCTGACCTCGAGTAGAC** CAAAAGGCCTCTTGTAAAGA&TGGTTTTCTGCCAATGACCAAACAGCCAAGATTTTCCTC STTTTCCGGAGAACATTTCTGACCAAAAGACGGTTACTGGTTTGTCGGTTCTAAAAGGAG TGCCACAGTAGAACTGTGTGAACAGAGAGCCCTTGTGGGTCCATGCTAACAAGACA **AACACTAAAGAAATTTTCTTACTGATATAATTAAATAAGGTGATTTTTTATAACAAAGACG** ACGGTGTCATCTTGACAGACACTTGTCTCTGGGAACACCCCAGGTACGATTGTTTCTGT TTGTGATTTCTTTAAAGAATGACTATATATTTTTTCCACTAAAAATATTTCTGC ATTCATTTTTATAGCAACAATTGGTAAACTCACTGTGATCAATATTTTATATCAT TTTACTCGATTCTAACATGACAAAAGGTCAAGTAGCTAAAAGATAATACCTTTTGACACA TAAGTAAAAATATCGTTGTTGATTAACCATTTTGAGTGACACTAGTTATAAAAATATAGTA 1321 1381 1441 1561 1621 1501

FIG. 2A	
ATNTFF KPPCVSVYRCGGCC	
CGCGACAAACACCTTCTTTAAACCTCCATGTGTGTCCGTCTACAGATGTGGGGGTTGCTG	301
RKTOCMPREVCIDVGKEFGV.	
GAGAAAGACTCAATGCCACGGGAGGTGTGTATAGATGTGGGGAAGGAGTTTGGAGT	241
TATAAAATTTGCTGCAGATTTATAATACAGAGATCTTGAAAAGTATTGATAATGAGTG	181
K G G W Q H N R E Q A N L N S R T E E T	
GAAAGGAGGCTGGCAACATAACAGAGAACAGGCCAACCTCAACTCAAGGACAGAGACAC	121
M T V L Y P E Y W K M Y K C Q L R	
AGATGAACTCATGACTGTACTCTACCCAGAATATTGGAAAATGTACAAGTGTCAGCTAAG	71
CGAGGCCACGCTTATGCAAGCAAAGATCTGGAGGAGCAGTTACGGTCTGTGTCCAGTGT ++++++	.

361	CAP	TAG	TGA	GGG	GCI	GC.	\GTC	3CA1	GAZ	CAC	CAG	CAC	GAG	CTA	CCT	CAATAGTGAGGGGCTGCAGTGCATGAACACCAGCACGAGCTACCTCAGCAAGACGTTATT	CAA	GACC	GTT	ATT +
	i Z		† 「 「 「 「	+ ט	I	0	÷ 0	Σ	z	F [- 	S E G L Q C M N T S T S Y	! !	່ຶ	: } +	1	LOCMNTSTSYLSKTL	F. ₩	E	IJ	Гч
421		AAT	TAC	AGT	၁၁၅	TCI	JCTC	TC	AGG	jacci	CAA	ACC	AGT	AAC	AAT	TGAAATTACAGTGCCTCTCTCTCAAGGCCCCCAAACCAGTAACAATCAGTTTTGCCAATCA	T.T.T.	TGC	CAA	TCA
	回	л I I З	-	+ >	۵	ו	+ S	S Q G	ט	П.	<u> </u>	l L L		1 !	1 1	PLSQGPKPVTISFANH	 - [ユム 	K	N	Ħ
481	CAC	TTC	CTG	S C C C C	ATG	CAI	GTC	TA	AACT	1357	TGT	TTA	CAG	ACA	AGT	CACTTCCTGCCGATGCTGTCTAAACTGGATGTTTACAGACAAGTTCATTCCATTATTAG	TTC	CAT	TAT	TAG
	E	T S C R	0	+ \	U	Σ	+ S	×		Ι.	>	 > 	N N	 0 	>	C M S K L D V Y R Q V H S I I R	S	Н	Н	- - 24
541	ACG	TTC	CCT	GCC	AGC	AAC	AC1	PACC	ACA	GTG	TCA	SSS	AGC	GAA	CAA	ACGTTCCCTGCCAGCACACTACCACAGTGTCAGGCAGCGAACAAGACCTGCCCCACCAA	CTG(CAC	CAA.
			S L P	1 1 +	A		+ 1	ام	Ø	U		 4	K	! ! Z +	 14	A T L P Q C Q A A N K T C P T N	 - -	<u>a</u> ,	£-	z
601	TTA	CAT	\mathtt{GTG}	GAA	TAA	TCA	CA1	בדטר:	CAG	ATC	CCI	၁၅၅	TCA	GGA	AGA	TTACATGTGGAATAATCACATCTGCAGATGCCTGGCTCAGGAAGATTTTATGTTTTCCTC	rat(TL	ITC	CTC
	>	Z	N M W	2	Z	H	- H	ט	R	Ü	1	4		 [1] 		Y M W N H I C R C L A Q E D F M F S S	+ Σ	[±,	S	S
661	GGA	TGC	TGG,	AGA	TGA	CTC	AAC	AGA	TGG	ATT	CCA	TGA	CAT	CTG	TGG	GGATGCTGGAGATGACTAGATGGATTCCATGACATGTGGACCAAACAAGGAGCT	AAA(CAA(3GA(3CT
	Ω	D A G D	į	- - -	0	i S	+ -		D S T D G	 - [24	 		! ! ⊢ !	ָ נ ל	ט	S T D G F H D I C G P N K E L	Z	×	ធ	
						-			L	FIG. 2B	2B									

FIG. 2C
P.C.T.N.R.Q.K.A.C.E.P.G.F.S.Y.S.E.E.V.C
1021 GCCATGTACGAACCGCCAGAAGGCTTGTGAGCCAGGATTTTCATATAGTGAAGTGTG
QKCLLKGKKFHHQTCSCYRR
Ţ
C P R N Q P L N P G K C A C E C T E S P
901 CTGCCCCAGAAATCAACCCCTAAATCCTGGAAAATGTGCCTGTGAATGTACAGAAAGTCC
Q C G A N R E F D E N T C Q C V C K R T
841 CCAATGTGGGGCCAACCGAGAATTTGATGAAAACACACATGCCAGTGTGTATGTA
H K E L D R N S C Q C V C K N K L F P S
781 CCACAAAGAACTAGACAGAACTCATGCCAGTGTGTCTGTAAAAAAAA
CCT

TAACTTTACAGAAATGGACTGGAGCTCATCTGCAAAAGGCCTCTTGTAAAGACTGGTTTT CTGCCAATGACCAAACAGCCAAGATTTTCCTCTTGTGATTTCTTTAAAAGAATGACTATA TCGTTGTGTCCCTTCATATTGGCAAAGACCACAAATGAGCTAAGATTGTACTGTTTTTCCA S Σ F16, 2D Ø 召 TTGTATTAAAAAAAAAAAAAAAA Ŏ 3 S C α 1081 1201 1141 1261 1321 1501 1381 1441

LGCGYLAHVL AEEAEIPREV IERLARSQIH SIRDLORLLE SLCCYLRLVS AEGDPIPEEL YEMLSDHSIR SFDDLORLLH SWVHWSLALL LY	Pdgfa IDSVGSEDSL DTSLRAHGVH ATKHVPEKRP LPIRRKRSIEEAVP Pdgfb GDP.GEEDGA ELDLNMTRSH SGGELES LARGRRSLG SLTIAEPAMI Vegf APMAEGGGQ NHHEVVKFMD .VYQR	Pdgfa AVCKTRTVIY EIPRSQVDPI SANFLIWPPC VEVKRCTGCC NTSSVKCOPS Pdgfb AECKTRTEVF EISRRLIDRI NANFLVWPPC VEVORCSGCC NNRNVOCRPT Vegf SYCHPIETLV DIFQEYPDEI EYIFKPSC VPLMRCGCCC NDEGLECVPT Vegf2 TQCMPREVCI DVGKEFGVATNTFFKPPC VSVYRCGGCC NSEGLQCMNT	Pdgfo RVHHRSVKVA KVEYVRKKPK LKEVQVRLEE HLEGAG AT Pdgfb QVQLRPVQVR KIEIVRKKPI FKKATVTLED HLACKG ETVAAARPVT Vegf EESNITMQIM RIK.PHQC QHIGEMSFLQ HNKCECRPKK DRARQEKKSV Vegf STSYLSKTLF EIT.VPLSQC PKPVTISFAN HTSQRQMSKL DVYRQVHSII
IERLARSOIH YEMLSOHSIR	LPIRRKRSI. LARGRRSLG. VYQR	VEVKRCTGCC VEVQRCSGCC VPLMRCGCCC VSVYRCGGCC	HLEGAG HLAGKO HNKGEGRPKK HTSGROMSKL
AEE AE I PREV AEGDP I PEEL L Y CQ	ATKHVPEKRP SGGELES NHHEVVKFMD YNTEILKSID	SANFL IMPPC NANFL VMPPC EY IFKPSC NTFFKPPC	LKEVQVRLEE FKKATVTLED QHIGEMSFLQ PKPVTISFAN
	51 Pdgfa IDSVGSEDSL DTSLRAHGVH ATKHVPEKRP LPIRRKRSI. Pdgfb GDP.GEEDGA ELDLNMTRSH SGGELES LARGRRSLG Vegf APMAEGGGQ NHHEVVKFMD .VYQR	E I PRSQVDP T E I SRRL I DR T D I F QE YPDE I DVGKE F GVA T	KVEYVRKKPK KIEIVRKKPI RIK.PHQC EIT.VPLSQC
1 Pdgfa .MRTLACLLL Pdgfb MNRCWA.LFL VegfMNFLL Vegf2MTV	51 IDSVGSEDSL GDP.GEEDGA APMAE	101 dgfa AVCKTRTVIY EIPRSQVDPT dgfb AECKTRTEVF EISRRLIDRT Vegf SYCHPIETLV DIFQEYPDEI egf2 TQCMPREVCI DVGKEFGVAT	151 RVHHRSVKVA OVOLRPVOVR EESNITMOIM STSYLSKTLF
Pdgfa Pdgfb Vegf Vegf2	Pdgfa Pdgfb Vegf Vegf	Pdgfa / Pdgfb / Vegf ? Vegf2 .	Pdgfa Pdgfb Vegf Vegf2

FIG. 3A

1.1/47

250 KHTH DKTALKETLG CLMPW SLPCPHP DFMFS SDAGDDSTDG	300	350 DKPRR	Pdgfa
GKHRKI VGARCO CLAQEI	RRKHL		SEEVCE
I RTVRVRRPPK GKHRKFKHTH C K KSRYKSWSVY VGARCCLMPW S I NYMMNHICR CLAQEDFMFS S			OKACEPGFSY
YREEDTDVR. AKTPOTRVT. GKGOKRKRP. CQAANKTCPT	LDEETCOCVC	LELNERICRC . EFDENTCQC	SCYRRPCTNR
201 PdgfaISLNPD YREEDIDVR. Pdgfb RSPGGSQEOR AKTPQTRVTI Vegf RGKGKGQKRKKK	251 Pdgfa Pdgfb A VegfCGP	Pdgfa	351 KGKKFHHQTC
Pdgfo Pdgfb P Vegf P Vegf P	Pdgfa Pdgfb Vegf Vegf	Pdgfa Pdgfb Vegf Vegf2	Pdgfa Pdgfb Vegf Vegf2

-16.3B

12/47

				·	
BETWEEN	VEGF2				
) identities Hown in thi E	VEGF				30.0
GENES IS S CLLWING TABI	PDGFβ			22.7	22.4
PERCENTAGE (%) OF AMINO ACID IDENTITIES BETWEEN EACH PAIR OF GENES IS SHOWN IN THE FOLLWING TABLE	PDGFα		48.0	20.7	23.5
PERCEN EA		PDGFa	PDGFB	VEGF	VEGF2

F16.4

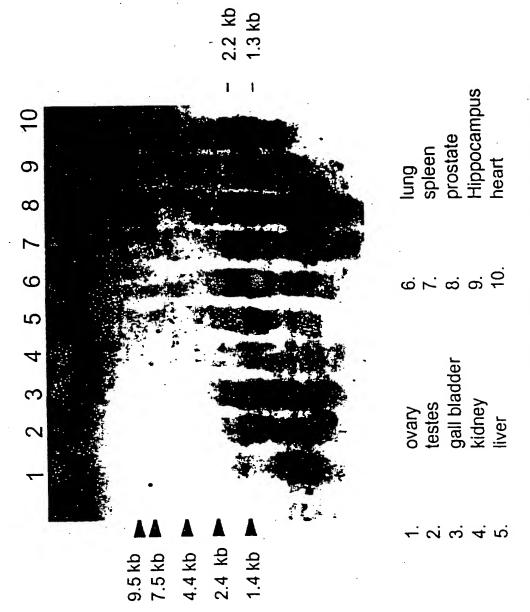
BEST AVAILABLE COPY

Expression of VEGF2 mRNA in Human Breast Tumor Cells



Lane 1. normal breast tissue Lane 2. breast tumor tissue Lane 3-9. breast tumor cell lines.

FIG.5

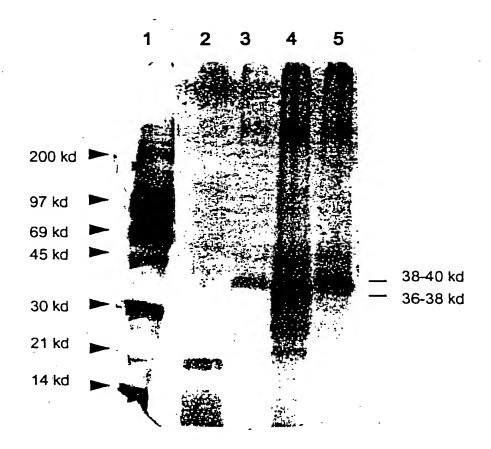


Expression of VEGF2 mRNA in human adult tissues.

FIG.6

BEST AVAILABLE COPY

15/47



Lane 1: 14-C and rainbow M.W. marker

Lane 2: FGF control

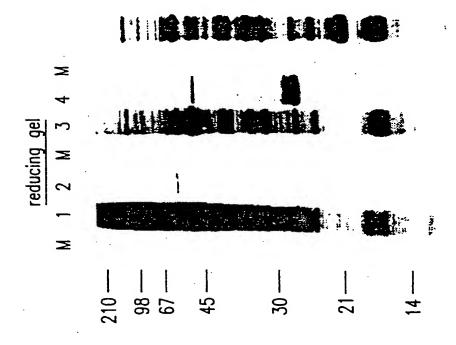
Lane 3: VEGF2 (M13-reverse \$ forward primers)
Lane 4: VEGF2 (M13-reverse & VEGF-F4 primers)
Lane 5: VEGF2 (M13-reverse & VEGF-F5 primers)

FIG.7

non-reducing gel

- 86

16/47



Marker vector Cytoplasm vector medium VEGF2 Cytoplasm VEGF2 medium

FIG.8B

Lane M: Lane 1: Lane 2: Lane 3: Lane 4:

vector medium VEGF2 medium

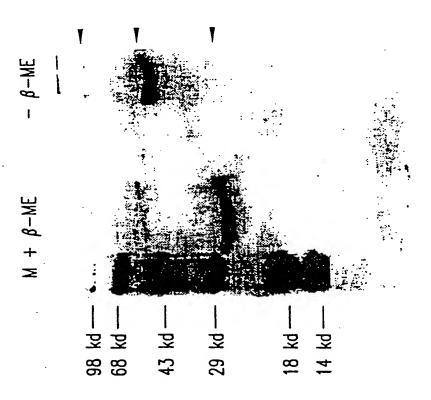
Lane Lane Lane

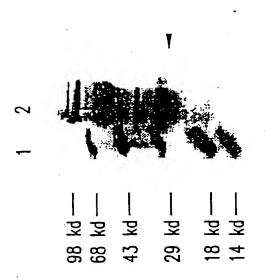
30

45

WO 99/46364

17/47





Molelular weight marker Precipitates containing VEGF2 Lane 1: Lane 2:

18/47

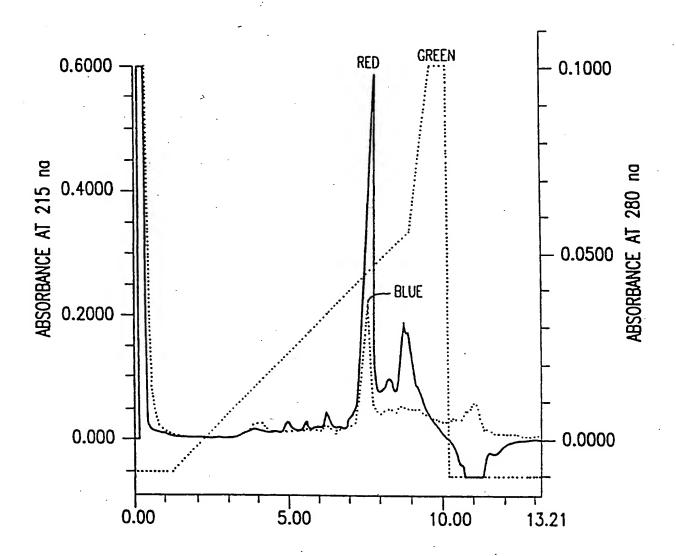
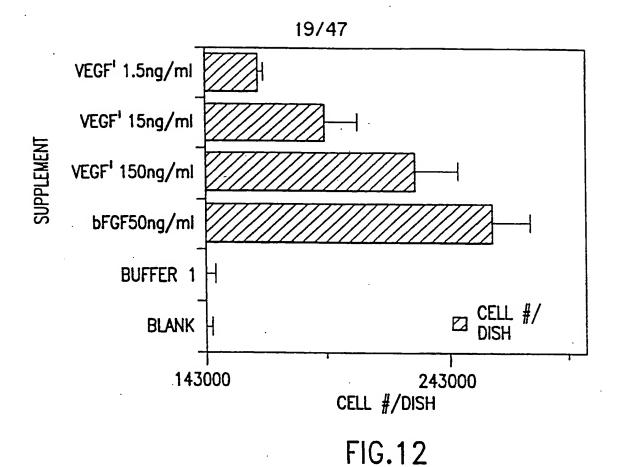


FIG. 11



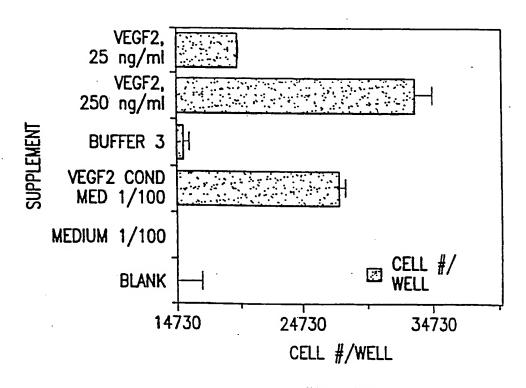


FIG.13

SUBSTITUTE SHEET (RULE 26)

BEST AVAILABLE COPY

20/47

tetal kidney
tetal lung
tetal lung
tetal liver
brain
b



FIG.14A

M B 1 2 3 4 5 6 7 8 9 10 11 12 13



FIG.14B

1. 2 3



2.4 kb





- 1.
- Molecular Weight Marker umbelical vein endothelial cells 2.
- 3. aortic smooth muscle cells
- Dermal fibroblast

FIG.15

22/47 及 5. vector control cell lysate 4. VEGF2-HA 3. control protein-HA 2. blank 1. m.w. marker 53 kd 2. VEGF2-HA conditioned medium 4. vector control 3. control protein-HA 2. blank 1. m.w. marker

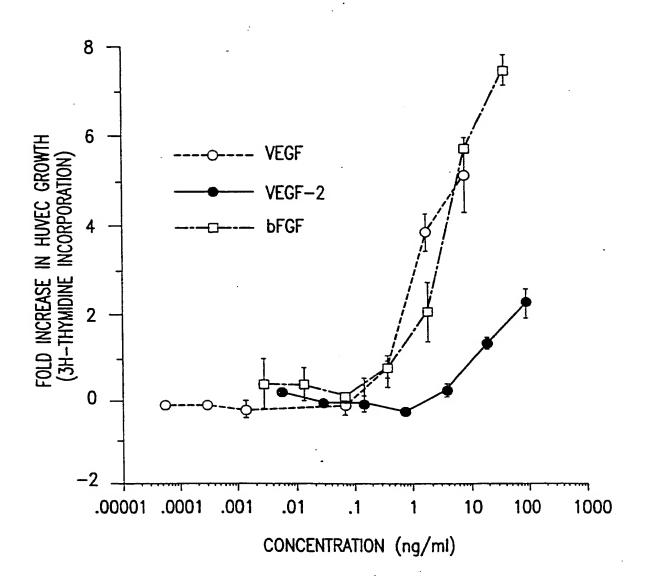


FIG.17

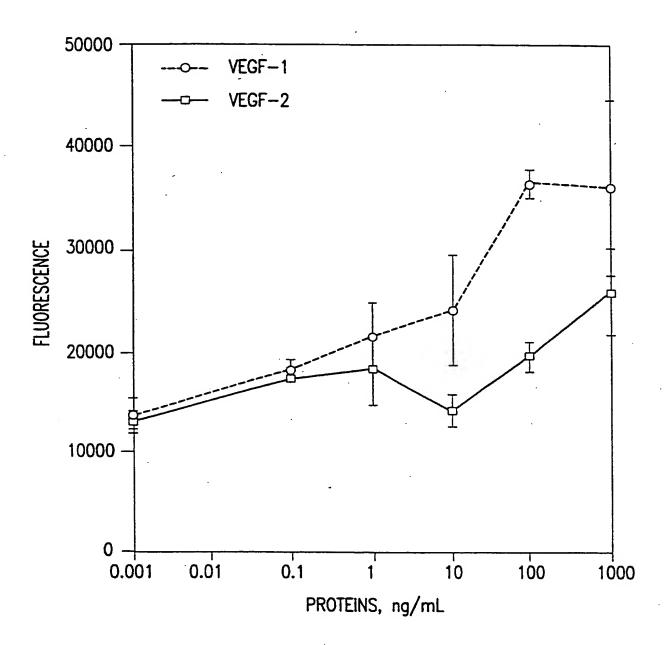


FIG.18

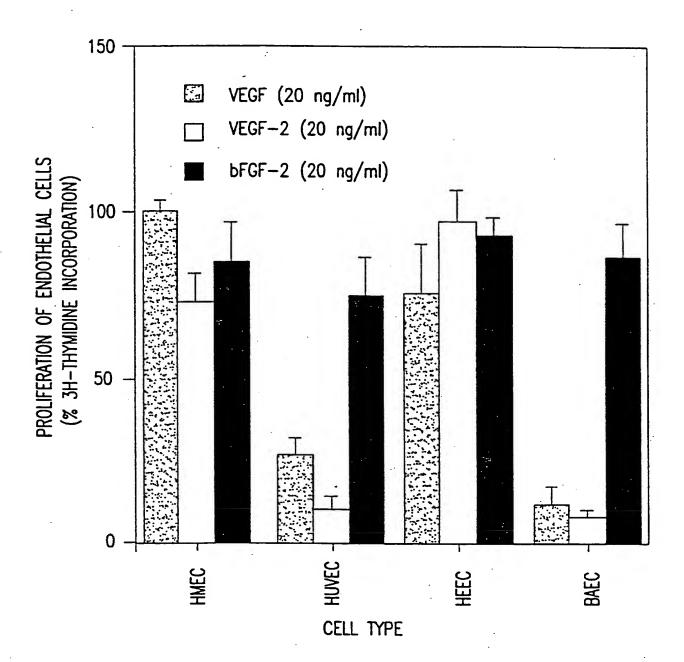


FIG.19

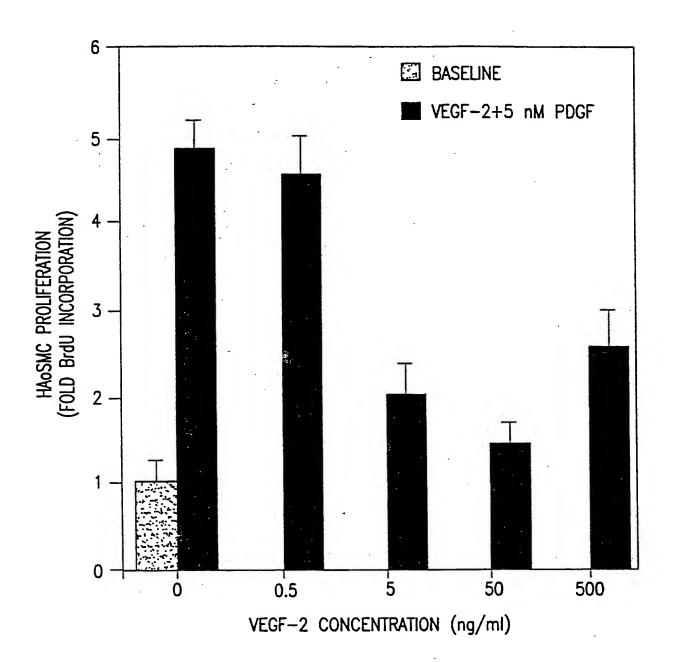


FIG.20A

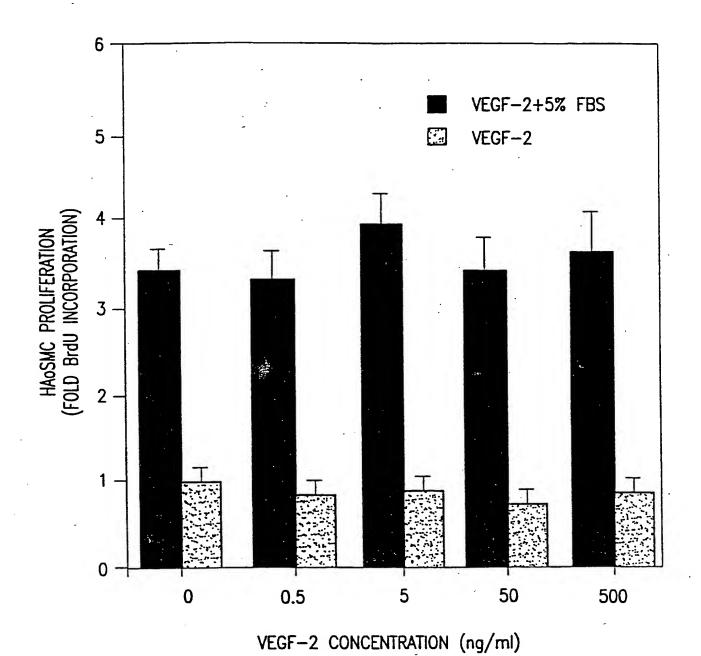
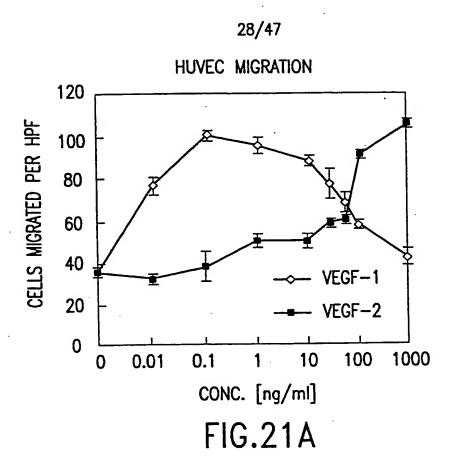


FIG.20B



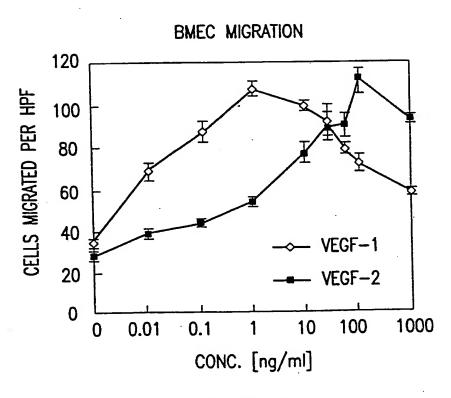


FIG.21B SUBSTITUTE SHEET (RULE 26)

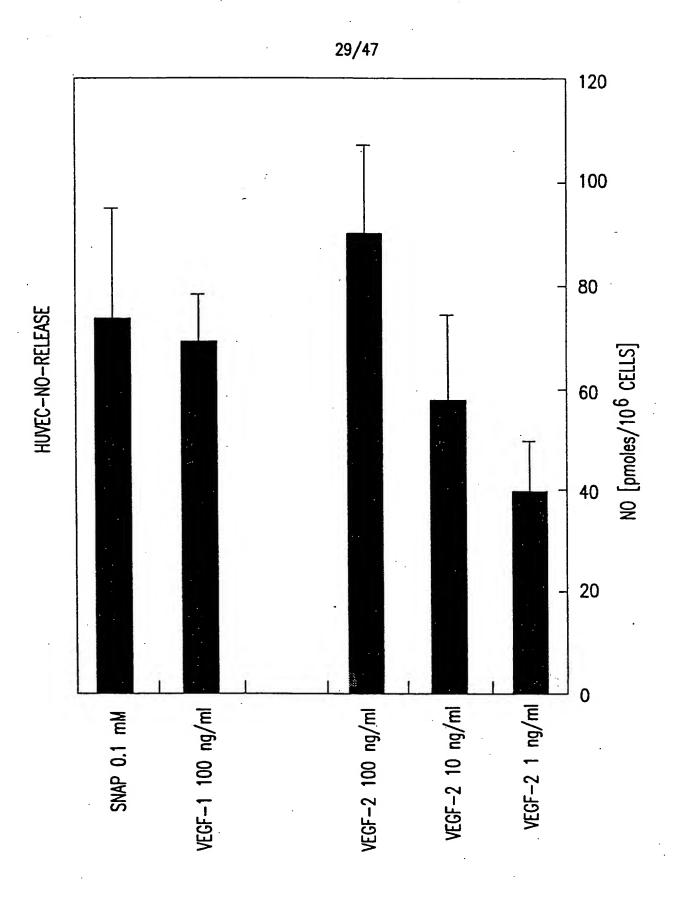
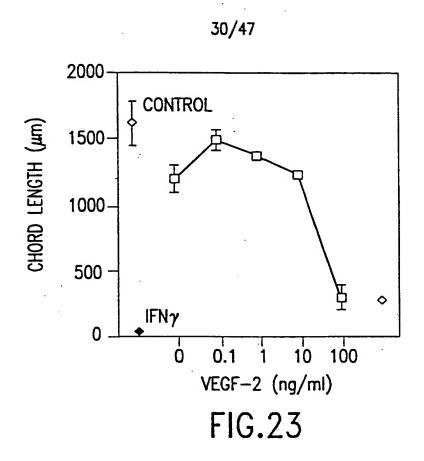


FIG. 22
SUBSTITUTE SHEET (RULE 26)



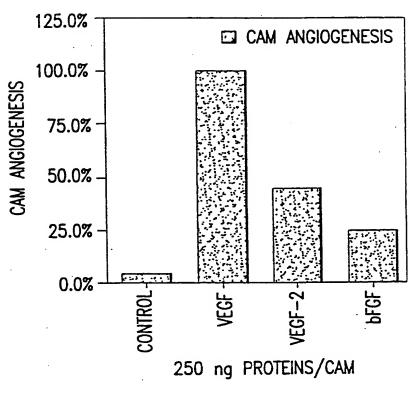
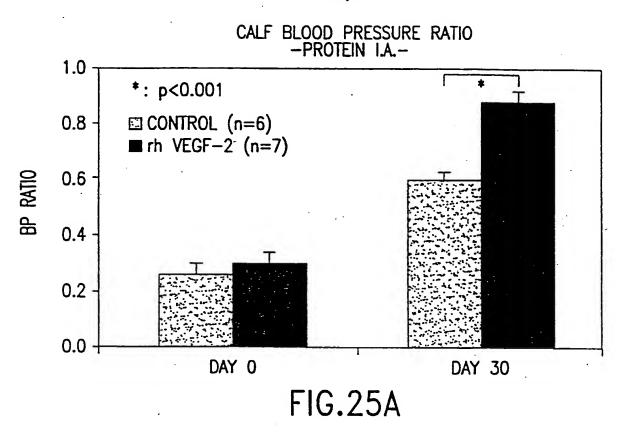
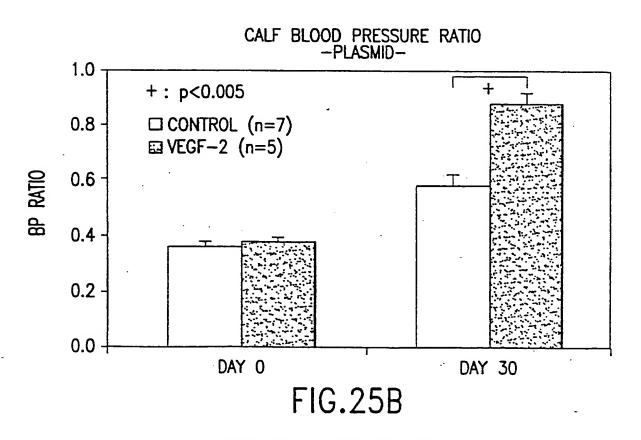


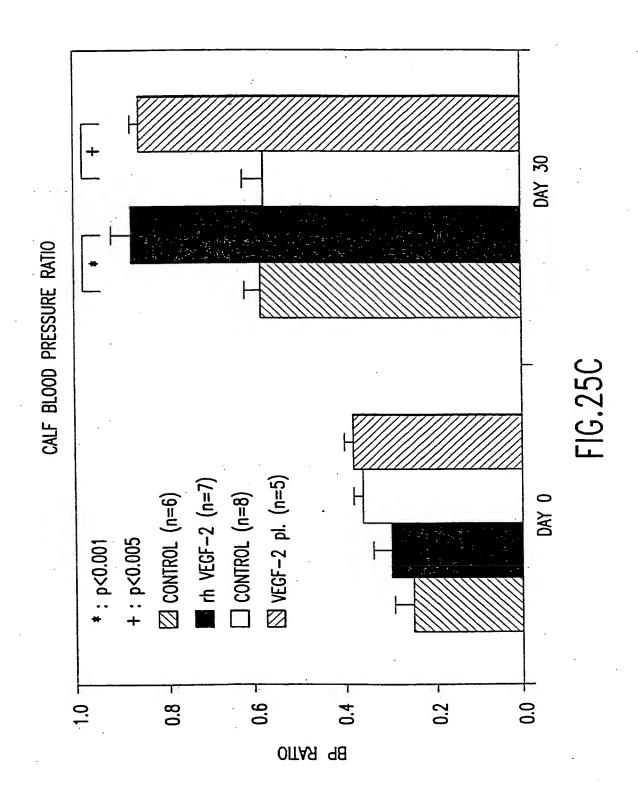
FIG. 24
SUBSTITUTE SHEET (RULE 26)

31/47

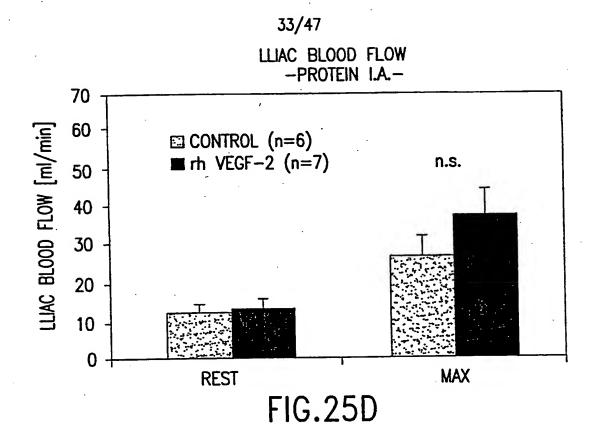


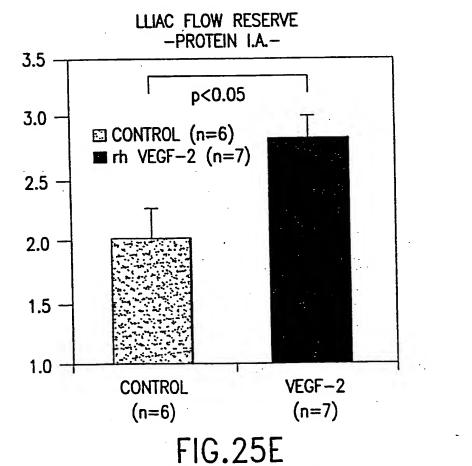


SUBSTITUTE SHEET (RULE 26)



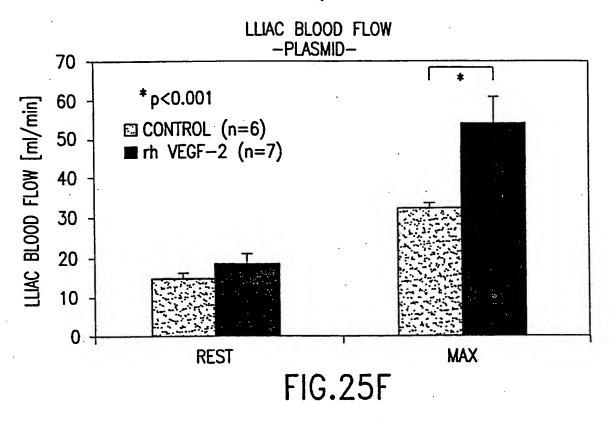
SUBSTITUTE SHEET (RULE 26)

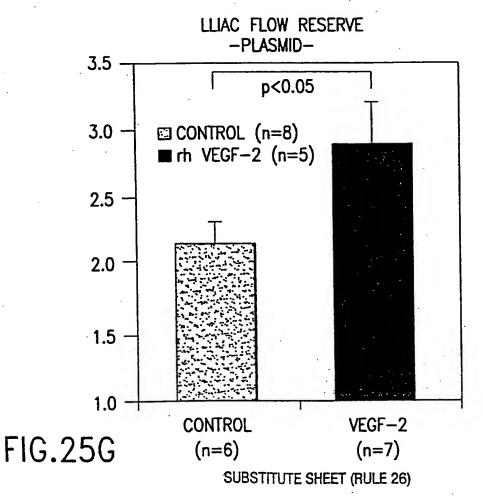




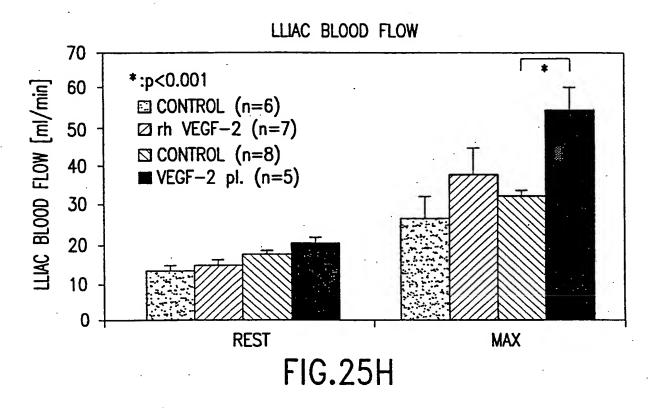
SUBSTITUTE SHEET (RULE 26)







35/47



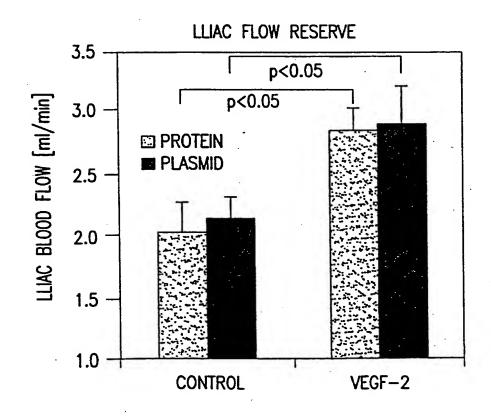
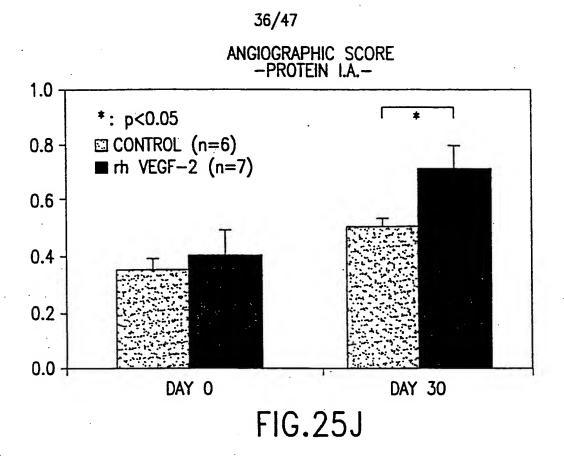
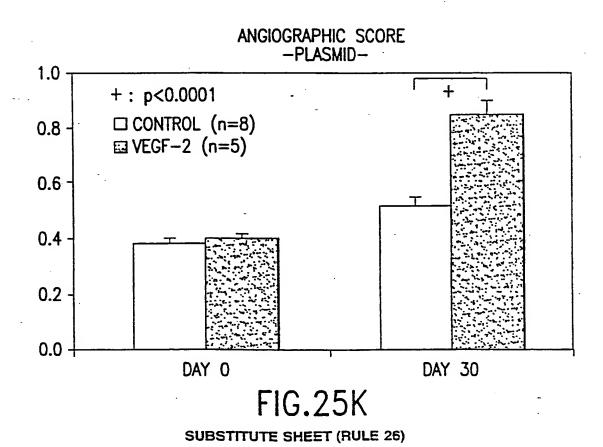
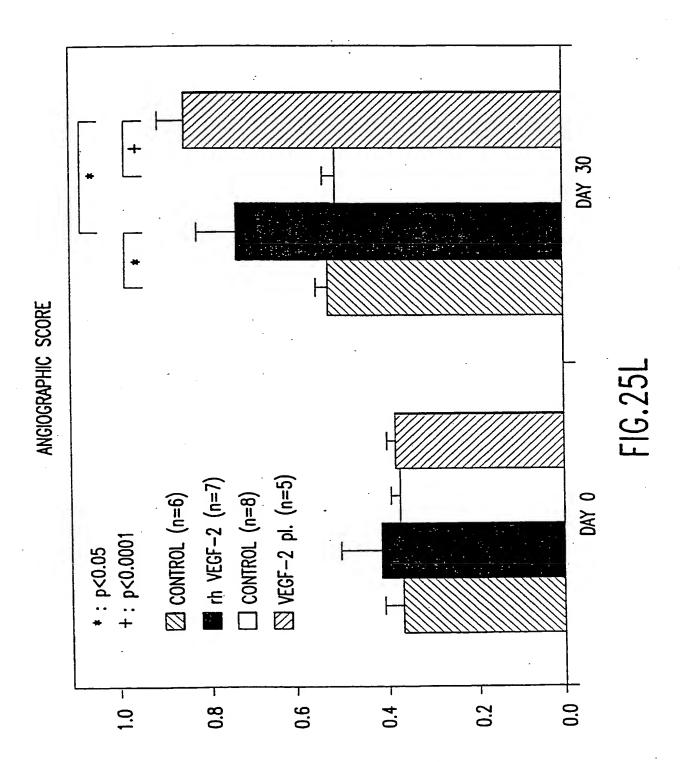


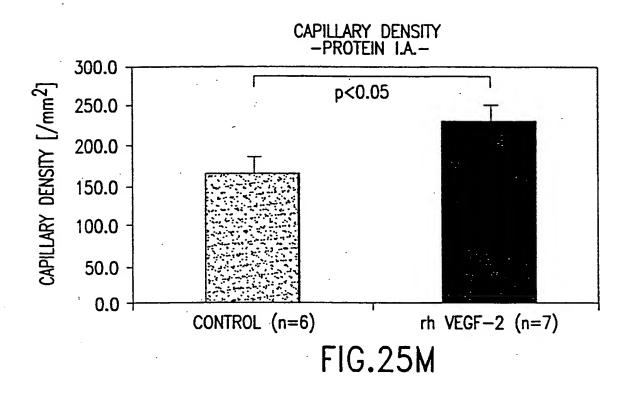
FIG. 251
SUBSTITUTE SHEET (RULE 26)

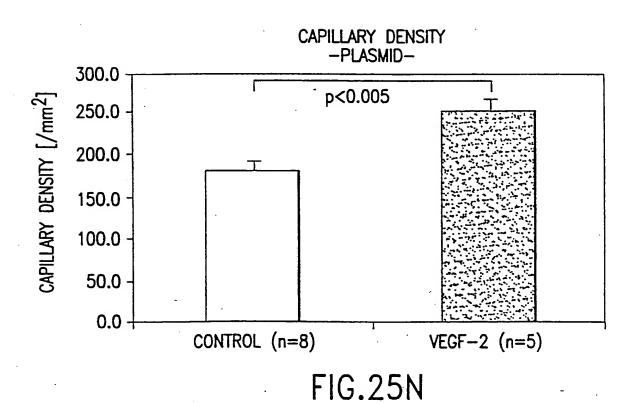




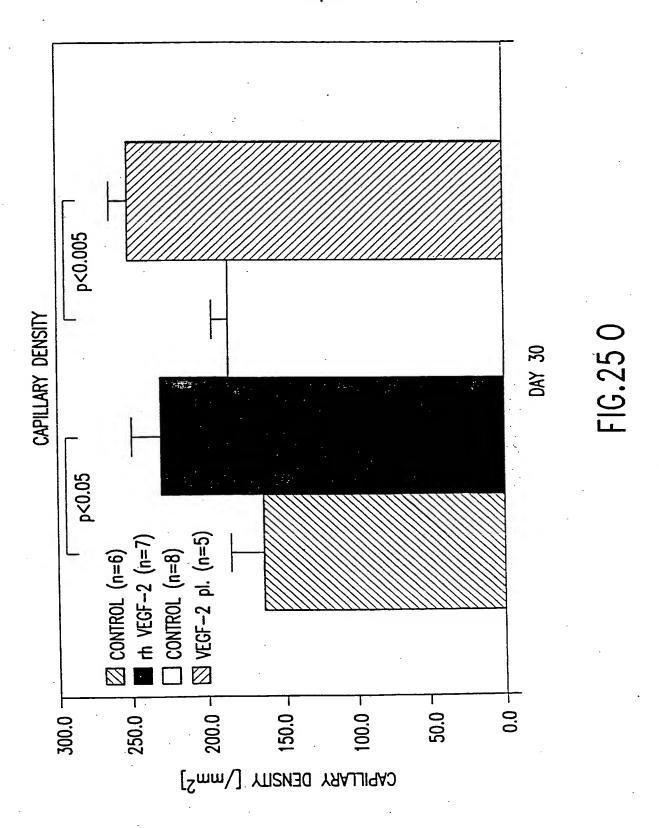


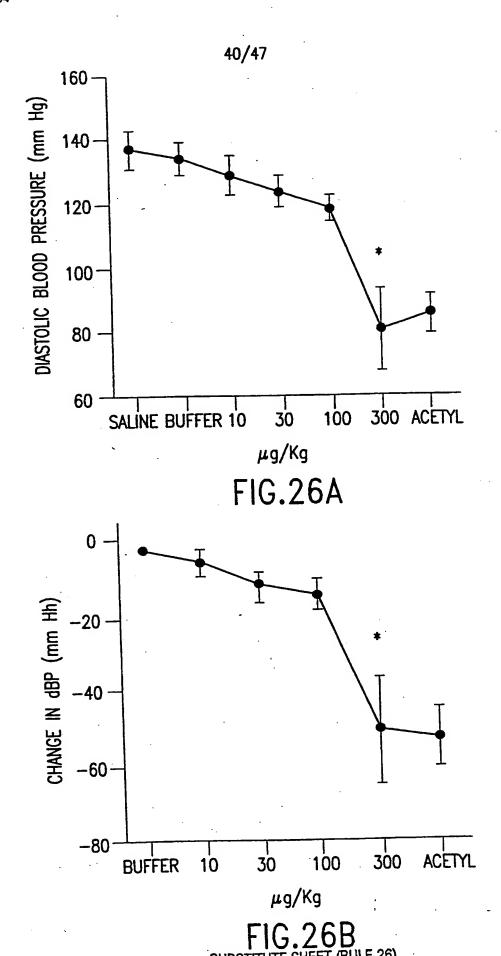
38/47





SUBSTITUTE SHEET (RULE 26)





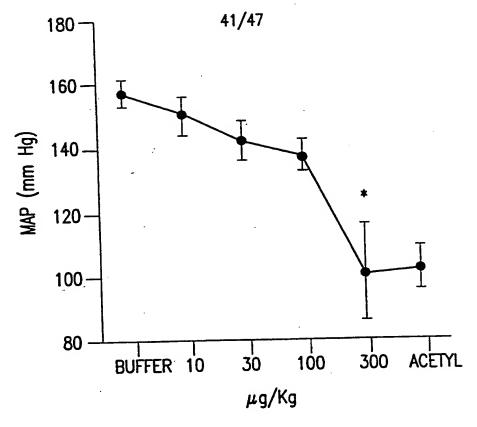


FIG.26C

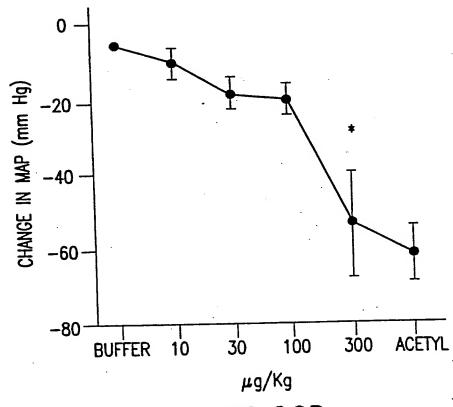
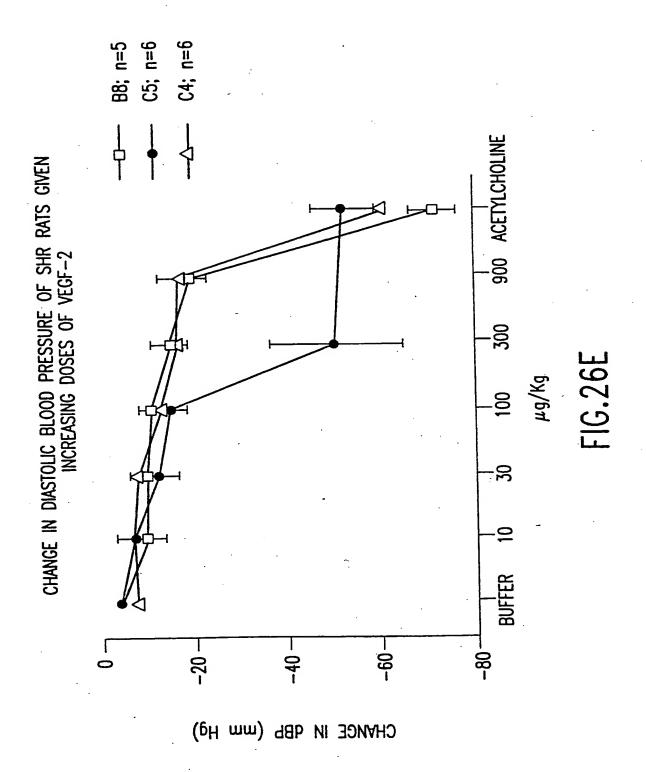
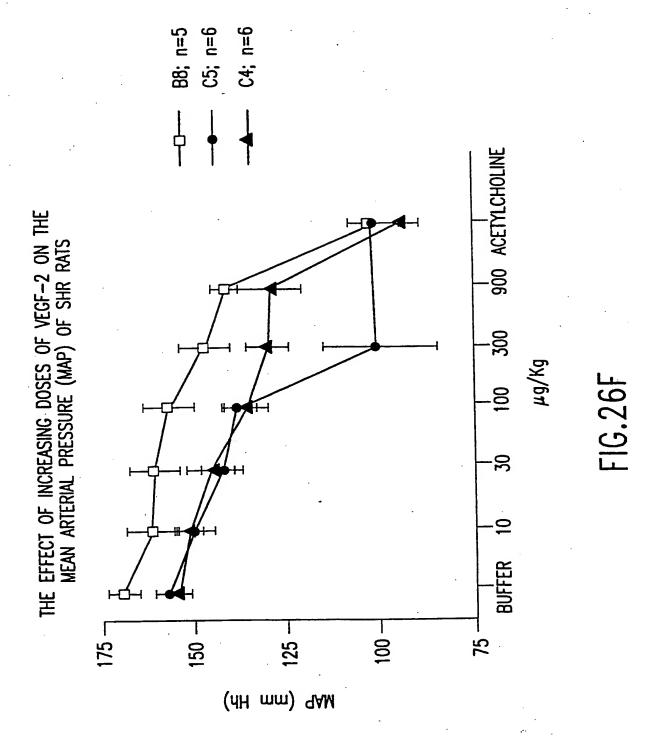
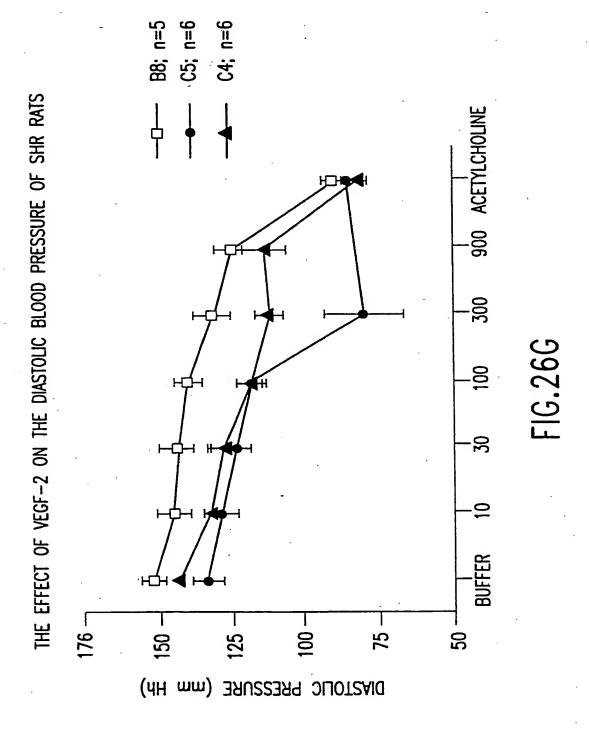


FIG.26D SUBSTITUTE SHEET (RULE 26)

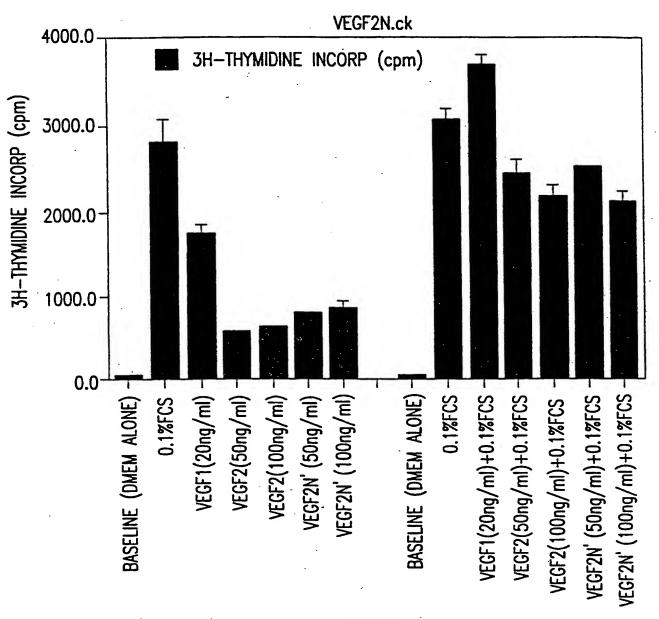






SUBSTITUTE SHEET (RULE 26)

45/47



TREATMENT

FIG.27

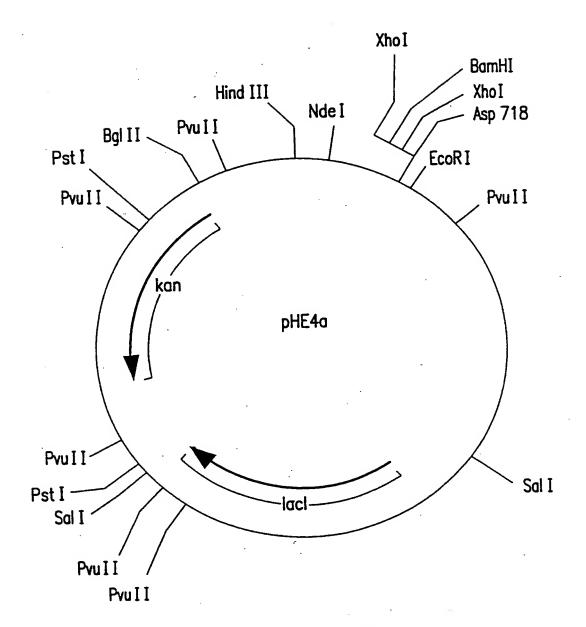


FIG.28

